Smart CARs engineered for cancer immunotherapy.

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Public Summary:
This review summarizes challenges for successfully translating chimeric antigen receptor (CAR)-engineered T cells for the treatment of hematological malignancies and solid cancers. We summarize important intrinsic variables, including CAR design and T-cell manufacturing, which are critical determinants of the overall safety and potency of the therapy. We also review extrinsic factors related to the tumor microenvironment that impact the ability of CAR T cells to penetrate the tumor, retain potency within the hostile tumor microenvironment and overcome antigen heterogeneity of the tumor. These challenges have spurred more complex CAR T-cell engineering strategies and combination therapies.

Scientific Abstract:
PURPOSE OF REVIEW: Chimeric antigen receptors (CARs) are synthetic immunoreceptors, which can redirect T cells to selectively kill tumor cells, and as 'living drugs' have the potential to generate long-term antitumor immunity. Given their recent clinical successes for the treatment of refractory B-cell malignancies, there is a strong push toward advancing this immunotherapy to other hematological diseases and solid cancers. Here, we summarize the current state of the field, highlighting key variables for the optimal application of CAR T cells for cancer immunotherapy. RECENT FINDINGS: Advances in CAR T-cell therapy have highlighted intrinsic CAR design and T-cell manufacturing methods as critical components for maximal therapeutic success. Similarly, addressing the unique extrinsic challenges of each tumor type, including overcoming the immunosuppressive tumor microenvironment and tumor heterogeneity, and mitigating potential toxicity, will dominate the next wave of CAR T-cell development. SUMMARY: CAR T-cell therapeutic optimization, including intrinsic and extrinsic factors, is critical to developing effective CAR T-cell therapies for cancer. The excitement of CAR T-cell immunotherapy has just begun, and will continue with new insights revealed in laboratory research and in ongoing clinical investigations.